

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No: 124-688

In re patent application of

Elmore, Michael J. et al.

Serial No. 08/981,087

Filed: May 27, 1998

For: TYPE F BOTULINUM TOXIN AND USE THEREOF



STATEMENT TO SUPPORT FILING AND SUBMISSION IN  
ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

Assistant Commissioner for Patents  
Washington, D.C. 20231  
Box SEQUENCE

Sir:

In connection with a Sequence Listing submitted concurrently herewith, the undersigned hereby states that:

1. the submission, filed herewith in accordance with 37 C.F.R. § 1.821(g), does not include new matter;

2. the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same; and

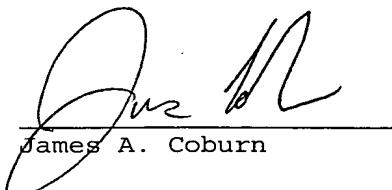
3. all statements made herein of their own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Respectfully submitted,

Sept. 4, 1999

Date

  
\_\_\_\_\_  
James A. Coburn

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1  
SEQUENCE LISTING

## (1) GENERAL INFORMATION:

(i) APPLICANT: Elmore, Michael J.  
Mauchline, Margaret L.  
Minton, Nigel P.  
Pasechnik, Vladimir A.  
Titball, Richard W.

(ii) TITLE OF INVENTION: TYPE F BOTULINUM TOXIN AND USE THEREOF

(iii) NUMBER OF SEQUENCES: 6

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: NIXON & VANDERHYE P.C.  
(B) STREET: 1100 North Glebe Rd. 8th floor  
(C) CITY: Arlington  
(D) STATE: VA  
(E) COUNTRY: USA  
(F) ZIP: 22201-4741

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk  
(B) COMPUTER: IBM PC compatible  
(C) OPERATING SYSTEM: PC-DOS/MS-DOS  
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: US 08/981,087  
(B) FILING DATE: 27-MAY-1998  
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: PCT/GB96/01409  
(B) FILING DATE: 12-JUN-1996

(viii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: GB 9511909.5  
(B) FILING DATE: 12-JUN-1995

(ix) ATTORNEY/AGENT INFORMATION:

(A) NAME: Crawford, Arthur R.  
(B) REGISTRATION NUMBER: 25,327  
(C) REFERENCE/DOCKET NUMBER: 124-688

(x) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: 703-816-4000  
(B) TELEFAX: 703-816-4100

## (2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 431 amino acids  
(B) TYPE: amino acid  
(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Ser	Tyr	Thr	Asn	Asp	Lys	Ile	Leu	Ile	Leu	Tyr	Phe	Asn	Lys	Leu	Tyr
1					5				10				15		
Lys	Lys	Ile	Lys	Asp	Asn	Ser	Ile	Leu	Asp	Met	Arg	Tyr	Glu	Asn	Asn
							20		25			30			
Lys	Phe	Ile	Asp	Ile	Ser	Gly	Tyr	Gly	Ser	Asn	Ile	Ser	Ile	Asn	Gly
						35		40			45				
Asp	Val	Tyr	Ile	Tyr	Ser	Thr	Asn	Arg	Asn	Gln	Phe	Gly	Ile	Tyr	Ser
						50		55			60				
Ser	Lys	Pro	Ser	Glu	Val	Asn	Ile	Ala	Gln	Asn	Asn	Asp	Ile	Ile	Tyr
65					70				75				80		
Asn	Gly	Arg	Tyr	Gln	Asn	Phe	Ser	Ile	Ser	Phe	Trp	Val	Arg	Ile	Pro
					85				90			95			
Lys	Tyr	Phe	Asn	Lys	Val	Asn	Leu	Asn	Asn	Glu	Tyr	Thr	Ile	Ile	Asp
					100			105				110			
Cys	Ile	Arg	Asn	Asn	Asn	Ser	Gly	Trp	Lys	Ile	Ser	Leu	Asn	Tyr	Asn
					115			120			125				
Lys	Ile	Ile	Trp	Thr	Leu	Gln	Asp	Thr	Ala	Gly	Asn	Asn	Gln	Lys	Leu
					130		135			140					
Val	Phe	Asn	Tyr	Thr	Gln	Met	Ile	Ser	Ile	Ser	Asp	Tyr	Ile	Asn	Lys
145					150				155			160			
Trp	Ile	Phe	Val	Thr	Ile	Thr	Asn	Asn	Arg	Leu	Gly	Asn	Ser	Arg	Ile
					165				170			175			
Tyr	Ile	Asn	Gly	Asn	Leu	Ile	Asp	Glu	Lys	Ser	Ile	Ser	Asn	Leu	Gly
					180			185			190				
Asp	Ile	His	Val	Ser	Asp	Asn	Ile	Leu	Phe	Lys	Ile	Val	Gly	Cys	Asn
					195			200			205				
Asp	Thr	Arg	Tyr	Val	Gly	Ile	Arg	Tyr	Phe	Lys	Val	Phe	Asp	Thr	Glu
					210		215			220					
Leu	Gly	Lys	Thr	Glu	Ile	Glu	Thr	Leu	Tyr	Ser	Asp	Glu	Pro	Asp	Pro
225					230				235				240		
Ser	Ile	Leu	Lys	Asp	Phe	Trp	Gly	Asn	Tyr	Leu	Leu	Tyr	Asn	Lys	Arg
					245				250			255			

Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn  
 260 265 270  
 Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro  
 275 280 285  
 Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile Ile  
 290 295 300  
 Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg  
 305 310 315 320  
 Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu Tyr  
 325 330 335  
 Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile Lys  
 340 345 350  
 Leu Ile Arg Thr Ser Asn Ser Asn Asn Ser Leu Gly Gln Ile Ile Val  
 355 360 365  
 Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn Asn  
 370 375 380  
 Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val Ala  
 385 390 395 400  
 Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn Gly  
 405 410 415  
 Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn  
 420 425 430

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 144 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu Tyr  
 1 5 10 15  
 Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn Asn  
 20 25 30  
 Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn Gly  
 35 40 45

Asp	Val	Tyr	Ile	Tyr	Ser	Thr	Asn	Arg	Asn	Gln	Phe	Gly	Ile	Tyr	Ser
50					55						60				
Ser	Lys	Pro	Ser	Glu	Val	Asn	Ile	Ala	Gln	Asn	Asn	Asp	Ile	Ile	Tyr
65				70					75				80		
Asn	Gly	Arg	Tyr	Gln	Asn	Phe	Ser	Ile	Ser	Phe	Trp	Val	Arg	Ile	Pro
				85					90				95		
Lys	Tyr	Phe	Asn	Lys	Val	Asn	Leu	Asn	Asn	Glu	Tyr	Thr	Ile	Ile	Asp
					100			105				110			
Cys	Ile	Arg	Asn	Asn	Asn	Ser	Gly	Trp	Lys	Ile	Ser	Leu	Asn	Tyr	Asn
					115			120				125			
Lys	Ile	Ile	Trp	Thr	Leu	Gln	Asp	Thr	Ala	Gly	Asn	Asn	Gln	Lys	Leu
					130		135					140			

## (2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 144 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Val	Phe	Asn	Tyr	Thr	Gln	Met	Ile	Ser	Ile	Ser	Asp	Tyr	Ile	Asn	Lys
1					5				10				15		
Trp	Ile	Phe	Val	Thr	Ile	Thr	Asn	Asn	Arg	Leu	Gly	Asn	Ser	Arg	Ile
					20			25				30			
Tyr	Ile	Asn	Gly	Asn	Leu	Ile	Asp	Glu	Lys	Ser	Ile	Ser	Asn	Leu	Gly
					35		40				45				
Asp	Ile	His	Val	Ser	Asp	Asn	Ile	Leu	Phe	Lys	Ile	Val	Gly	Cys	Asn
					50		55			60					
Asp	Thr	Arg	Tyr	Val	Gly	Ile	Arg	Tyr	Phe	Lys	Val	Phe	Asp	Thr	Glu
					65		70		75		80				
Leu	Gly	Lys	Thr	Glu	Ile	Glu	Thr	Leu	Tyr	Ser	Asp	Glu	Pro	Asp	Pro
					85		90				95				
Ser	Ile	Leu	Lys	Asp	Phe	Trp	Gly	Asn	Tyr	Leu	Leu	Tyr	Asn	Lys	Arg
					100		105				110				
Tyr	Tyr	Leu	Leu	Asn	Leu	Leu	Arg	Thr	Asp	Lys	Ser	Ile	Thr	Gln	Asn
					115		120				125				

Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro  
 130 135 140

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 143 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile Ile  
 1 5 10 15

Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg  
 20 25 30

Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu Tyr  
 35 40 45

Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile Lys  
 50 55 60

Leu Ile Arg Thr Ser Asn Ser Asn Asn Ser Leu Gly Gln Ile Ile Val  
 65 70 75 80

Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn Asn  
 85 90 95

Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val Ala  
 100 105 110

Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn Gly  
 115 120 125

Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn  
 130 135 140

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1293 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

TCATATACTA ATGATAAAAT TCTAATTAA TATTTAATA AATTATATAA AAAAATTAAA	60
GATAACTCTA TTTAGATAT GGGATATGAA AATAATAAAT TTATAGATAT CTCTGGATAT	120
GGTTCAAATA TAAGCATTAA TGGAGATGTA TATATTTATT CAACAAATAG AAATCAATT	180
GGAATATATA GTAGTAAGCC TAGTGAAGTT AATATAGCTC AAAATAATGA TATTATATAC	240
AATGGTAGAT ATCAAAATT TAGTATTAGT TTCTGGTAA GGATTCCCTAA ATACTTCAAT	300
AAAGTGAATC TTAATAATGA ATATACTATA ATAGATTGTA TAAGGAATAA TAATTCAAGGA	360
TGGAAAATAT CACTTAATTA TAATAAAATA ATTTGGACTT TACAAGATAC TGCTGGAAAT	420
AATCAAAAC TAGTTTTAA TTATACACAA ATGATTAGTA TATCTGATTA TATAAATAAA	480
TGGATTTTG TAACTATTAC TAATAATAGA TTAGGCAATT CTAGAATTAA CATCAATGGA	540
AATTTAATAG ATGAAAAATC AATTCGAAT TTAGGTGATA TTCATGTTAG TGATAATATA	600
TTATTTAAAA TTGTTGGTTG TAATGATACA AGATATGTTG GTATAAGATA TTTTAAAGTT	660
TTTGATACGG AATTAGGTAA AACAGAAATT GAGACTTTAT ATAGTGATGA GCCAGATCCA	720
AGTATCTAA AAGACTTTG GGGAAATTAT TTGTTATATA ATAAAAGATA TTATTTATTG	780
AATTTACTAA GAACAGATAA GTCTATTACT CAGAATTCAA ACTTTCTAAA TATTAATCAA	840
CAAAGAGGTG TTTATCAGAA ACCAAATATT TTTTCCAACA CTAGATTATA TACAGGAGTA	900
GAAGTTATTA TAAGAAAAAA TGGATCTACA GATATATCTA ATACAGATAA TTTTGTAGA	960
AAAAATGATC TGGCATATAT TAATGTAGTA GATCGTGATG TAGAATATCG GCTATATGCT	1020
GATATATCAA TTGCAAAACC AGAGAAAATA ATAAAATTAA TAAGAACATC TAATTCAAAC	1080
AATAGCTTAG GTCAAATTAT AGTTATGGAT TCAATAGGAA ATAATTGCAC AATGAATT	1140
CAAAACAATA ATGGGGCAA TATAGGATTA CTAGGTTTTC ATTCAAATAA TTTGGTTGCT	1200
AGTAGTTGGT ATTATAACAA TATACGAAAA AATACTAGCA GTAATGGATG CTTTTGGAGT	1260
TTTATTTCTA AAGAGCATGG ATGGCAAGAA AAC	1293

## (2) INFORMATION FOR SEQ ID NO:6:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1313 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

GGATCCATAT GTCTTACACT AACGACAAAA TCCTGATCCT GTACTTCAAC AACTGTACA 60  
 AAAAAATCAA AGACAACCTCT ATCCTGGACA TGCCTTACGA AAACAACAAA TTCATCGACA 120  
 TCTCTGGCTA TGGTTCTAAC ATCTCTATCA ACGGTGACGT CTACATCTAC TCTACTAAC 180  
 GCAACCAGTT CGGTATCTAC TCTTCTAAAC CGTCTGAAGT AAACATCGCT CAGAACAAACG 240  
 ACATCATCTA CAACGGTCGT TACCAAACT TCTCTATCTC TTTCTGGGTT CGTATCCCGA 300  
 AATACTTCAA CAAAGTTAAC CTGAACAAACG AATACACTAT CATCGACTGC ATCCGTAACA 360  
 ACAACTCTGG TTGGAAAATC TCTCTGAACt ACAACAAAAT CATCTGGACT CTGCAGGACA 420  
 CTGCTGGTAA CAACCAGAAA CTGGTTTCA ACTACACTCA GATGATCTCT ATCTCTGACT 480  
 ACATTAATAA ATGGATCTTC GTTACTATCA CTAACAAACCG TCTGGTAAAC TCTCGTATCT 540  
 ACATCAACGG TAACCTGATC GATGAAAAAT CTATCTCTAA CCTGGGTGAC ATCCACGTT 600  
 CTGACAACAT CCTGTTCAAA ATCGTTGGTT GCAACGACAC GCGTTACGTT GGTATCCGTT 660  
 ACTTCAAAGT TTTCGACACT GAACTGGGTAA AACTGAAAT CGAAACTCTG TACTCTGACG 720  
 AACCGGACCC GTCTATCCTG AAAGACTTCT GGGGTAACt CCTGCTGTAC AACAAACGTT 780  
 ACTACCTGCT GAACCTGCTC CGGACTGACA AATCTATCAC TCAGAACTCT AACTTCCTGA 840  
 ACATCAACCA GCAGCGTGGT GTTTATCAGA AACCTAATAT CTTCTCTAAC ACTCGTCTGT 900  
 ACAACTGGTGT TGAAGTTATC ATCCGTAAAA ACGTTCTAC TGACATCTCT AACACTGACA 960  
 ACTTCGTACG TAAAAACGAC CTGGCTTACA TCAACGTTGT TGACCGTGAC GTTGAATACC 1020  
 GTCTGTACGC TGACATCTCT ATCGCTAAAC CGGAAAAAAT CATCAAACGT ATCCGTACTT 1080  
 CTAACTCTAA CAACTCTCTG GGTCAGATCA TCGTTATGGA CTCGATCGGT AACAAACTGCA 1140  
 CTATGAACCTT CCAGAACAAAC AACGGTGGTA ACATCGGTCT GCTGGTTTC CACTCTAAC 1200  
 ACCTGGTTGC TTCTTCTTGG TACTACAACA ACATCCGTAA AAACACTTCT TCTAACGGTT 1260  
 GCTTCTGGTC TTTCATCTCT AAAGAACACG GTTGGCAGGA AAAACTAATCT AGA 1313

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING  
NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

7. Other: \_\_\_\_\_

**Applicant Must Provide:**

An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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